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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/358,141      | 07/20/1999  | JEFFREY R. SAMPSON   | 10990393-1          | 1170             |

22878 7590 06/13/2005

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EXAMINER

ZARA, JANE J

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1635

DATE MAILED: 06/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 09/358,141             | SAMPSON, JEFFREY R. |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | Jane Zara              | 1635                |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 June 2004 and 11 March 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 10-18 and 25-35 is/are pending in the application.
- 4a) Of the above claim(s) 10-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 25-35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

This Office action is in response to the communication filed 6-18-04 and 3-11-05.

Claims 1, 10-18, 25-35 are pending in the instant application.

### ***Election/Restrictions***

This application contains claims 10-18 drawn to an invention nonelected with traverse in the election filed 2-19-02. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

### ***Response to Arguments and Amendments***

#### **Withdrawn Rejections**

Any rejections not repeated in this Office action are hereby withdrawn.

#### **Maintained Rejections**

Claims 1 and 25-35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-26 of copending Application No. 09/632,639 for the reasons of record set forth in the Office action mailed 12-17-03.

No arguments have been made addressing this rejection.

Claims 1 and 25-34 are rejected under 35 U.S.C. 102(e) as being anticipated by Vivekananda et al for the reasons of record set forth in the Office action mailed 12-17-03.

Applicant's arguments filed 6-18-04 have been fully considered but they are not fully persuasive. Applicants argue that Vivekananda et al do not teach methods of synthesizing nucleic acid molecules with reduced secondary structure, but instead disclose a method of detecting anthrax spores and other chemical and biological agents by utilizing nucleic acid molecules that are able to specifically bind particular targets including through non-Watson-Crick interactions. Applicants argue further that Vivekananda et al define preferred nucleic acid aptamers as nucleic acids that bind to other molecules which do not encompass standard nucleic acid hydrogen bond formation exemplified by Watson-Crick base pair formation, but instead encompass all other types of non-covalent binding. Applicants are correct that Vivekananda et al teach aptamers as a preferred embodiment. But, contrary to Applicants' assertions, the fact that aptamers are a preferred embodiment does not preclude Vivekananda as prior art of the instantly claimed invention. In columns 20-24, 29-31, Vivekananda et al teach the synthesis of nucleic acid ligands that contain modified nucleotides that render intra-strand, complementary nucleotides with a reduced ability to form stable hydrogen bonded base pairs. Vivekananda et al specifically disclose the incorporation of 2'-amino purines, 2'-thio substituted bases including 2'-thio cytosine and 2'-thio uridine, as well as the incorporation of inosine into nucleic acid ligands through various methods including PCR, RT-PCR, LCR, and several other nucleic acid amplification procedures.

Whether these resultant nucleic acid ligands are used for recognizing target viral or bacterial nucleic acid sequences, or instead are utilized for recognizing non-nucleic acid target molecules such as anthrax spores, Vivekananda et al nevertheless teach the instantly claimed methods of synthesizing nucleic acid polynucleotides with reduced secondary structure by incorporating the claimed modified bases, thereby producing nucleic acid strands with a reduced ability to form intra-molecular base pairs.

Claims 1 and 25-35 are rejected under 35 U.S.C. 102(e) as being anticipated by Kutayavin et al for the reasons of record set forth in the Office action mailed 12-17-03.

Applicant's arguments filed 6-18-04 have been fully considered but they are not persuasive. Applicants argue that Kutayavin et al is not proper prior art because they teach methods of producing polynucleotides with reduced ability to form inter-molecular base pairs, as opposed to the instantly claimed invention which teaches a method of producing polynucleotides with reduced ability to form intra-molecular base pairs. Applicants argue further that Kutayavin et al teach away from the instantly claimed invention because they require a matched set of oligonucleotide that are unable to hybridize with each other. Applicants are correct that Kutayavin et al teach methods of producing complementary nucleic acid strands with reduced ability to form intramolecular base pairs. Kutayavin et al disclose methods of synthesizing polynucleotides with a reduced ability to form self annealing double strands by incorporating the modified bases claimed, which in turn renders the polynucleotides with reduced ability to form stable hydrogen bonded base pairs with either a complementary strand or with complementary bases within the same strand (see e.g. col. 1 of Kutayavin

et al: "[t]he ODNs include modified bases of such nature that the modified base forms stable hydrogen bonded base pairs with the natural partner base, but does not form stable hydrogen bonded base pairs with its modified partner... The ODNs of the invention, however, form substantially stable hybrids with the target sequence in each strand of duplex nucleic acid." ). The procedure disclosed by Kutyaev, therefore, is indistinguishable from the instantly claimed methods because they both involve the synthesis of oligonucleotides in the presence of modified bases to produce nucleic acid with reduced ability to hybridize to complementary bases by reducing the ability to form Watson-Crick base pairing. This characteristic exists in intra-molecular as well as inter-molecular, complementary nucleic acid strands. Therefore Kutyaev et al properly anticipates the instantly claimed methods.

Furthermore, the distinction between inter-molecular and intra-molecular base complementarity that is repeatedly stressed by Applicant to distinguish the instantly claimed invention from the prior art is also addressed by Kutyaev et al, albeit within the context of the target sequence: "It is known that secondary structure of mRNA and ribosomal RNA do not have two strands in the strict sense of that term. Nevertheless, unless the context otherwise indicates, in the present description the terminology "two strands" of double stranded nucleic acids also refers to the two complementary portions of duplex mRNA or of duplex ribosomal RNA as well. The general concept of double stranded DNA and of secondary structure ... is covered in this description by the term "duplex nucleic acid." (see col. 4). For these reasons, the instant 102 rejections are maintained.

### ***Conclusion***

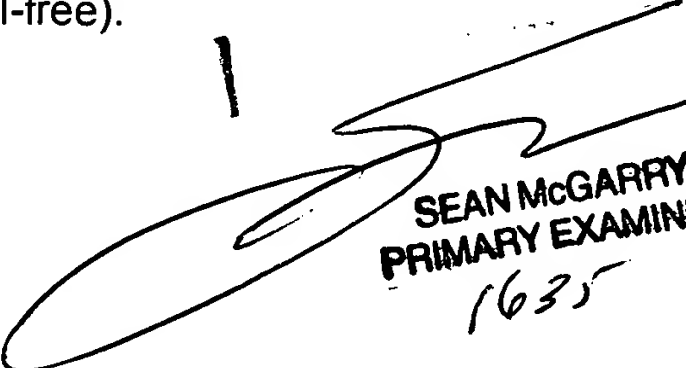
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. **NO DUPLICATE COPIES SHOULD BE SUBMITTED** so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765**. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
SEAN MCGARRY  
PRIMARY EXAMINER  
1635

JZ  
6-7-05